

One Wales Medicine Assessment Group summary of decision rationale

Medicine: vedolizumab (Entyvio®)

Indication: **Reassessment of OW22 to extend the indication to include grade 2 enterocolitis when symptoms have not responded to first-line immunosuppression with corticosteroids or in patients who are corticosteroid-dependent requiring multiple challenges with corticosteroids, and for enterocolitis grades 3-4 requiring multiple challenge with corticosteroids when symptoms have not responded to infliximab or when infliximab is unsuitable**

Meeting date: 19 August 2024

Criteria	OWMAG opinion
Clinical effectiveness	<p>OWMAG note that the current One Wales decision (OW22) recommends vedolizumab to treat ICI-induced enterocolitis grade 3–4 where symptoms have not responded to first-line immunosuppression with corticosteroids and infliximab, or when infliximab is unsuitable. This reassessment is in response to the 12-month review of OW22 which identified change to the European Society for Medical Oncology (ESMO) guidelines for treating ICI-induced enterocolitis. The One Wales Medicines Assessment Group (OWMAG) proposed that, in accordance with the new treatment guidelines, vedolizumab should be reassessed to include the treatment of ICI-induced grade 2 enterocolitis that had not responded first-line immunosuppression with corticosteroids. This proposal was supported by Welsh clinicians who also requested that patients with grades 2–4 enterocolitis who are corticosteroid-dependent requiring multiple challenges with corticosteroids be included in the expanded indication being considered.</p> <p>OWMAG note that there is limited new clinical effectiveness evidence to that already presented and considered as part of the original assessment and the 12-month review. New evidence presented that includes grade 2 enterocolitis is limited and consists of 3 retrospective studies and interim results of an ongoing clinical trial. For the treatment of grade 2 enterocolitis, the group notes that vedolizumab dosage used (when reported) was consistent with the 300 mg dose recommended in national and international guidelines while dosing schedule frequency varied with generally no more than three doses received. However, results were generally reported for the mixed colitis group (grades 1-4) with no stratification by grade and the treatment pathway varied between studies with vedolizumab given only after failure of infliximab in some. All studies showed a clinical benefit in terms of enterocolitis symptom improvement and partial or complete response to treatment with vedolizumab and reflected the results of previous studies.</p>

	<p>OWMAG also considered some real-world data submitted by Welsh clinicians and evidence provided by clinical experts, both in the ESR and at the meeting, who reported positive clinical outcomes for patients they had treated with vedolizumab. OWMAG noted that vedolizumab is the preferred treatment of choice over infliximab for grade 2 enterocolitis unresponsive to corticosteroids in the ESMO guidelines. This is due to its established gut-specificity which is particularly beneficial for the treatment of ICI-induced enterocolitis and, although it takes longer to elicit a response than infliximab, time to treatment success is less critical for moderate (i.e. grade 2) enterocolitis.</p> <p>Clinicians highlighted that the majority of patients with grade 2 enterocolitis unresponsive to steroid treatment progress to grade 3. At this point, such patients will become eligible for treatment with infliximab or vedolizumab via OW21 and OW22. Allowing use of vedolizumab earlier in the pathway prevents the worsening of symptoms and lessens steroid burden by allowing rapid steroid weaning. Clinicians also highlight that 90% of patients with grade 2 enterocolitis who are successfully treated with either infliximab or vedolizumab are able to resume their cancer treatment with ICIs; this compares to 25-33% of patients with grade 3 enterocolitis. The detrimental impact of the prolonged use of high dose corticosteroids was also discussed; this can result in a range of serious adverse events including some that are irreversible, prevention or delay of cancer-related treatments or surgery and a decrease in quality of life. Clinicians also highlight that some patients with enterocolitis are steroid-dependent and require multiple treatment courses with steroids for relapses. They note concerns regarding the increase risk of steroid-related adverse events due to repeated exposure and would welcome the option to use vedolizumab for these patients to prevent future relapses and lessen steroid burden.</p> <p>OWMAG note that no new safety signals have been observed for the use of vedolizumab to treat ICI-induced enterocolitis.</p> <p>OWMAG considers that the evidence provided demonstrated clinical effectiveness.</p>
Cost-effectiveness	<p>There is no published cost-effectiveness evidence available for vedolizumab for the extended indication. OWMAG considered the cost-consequence analysis, threshold analysis and scenario analyses presented.</p>

	<p>OWMAG acknowledged the limited scope of the analyses in terms of capturing all costs and effects, in particular longer term costs and effects.</p> <p>Clinicians shared their experiences in treating this patient group, suggesting that:</p> <ul style="list-style-type: none"> • the majority of patients not responding to corticosteroids would progress to grade 3 • if grade 2 patients are treated successfully, then approximately 90% can be rechallenged with ICI compared with 25% to 33% of patients who experience grade 3 ICI-induced enterocolitis • Grade 3 patients tend to be treated as day-cases rather than in-patients • Monitoring is intensive for patients with steroid burden • ICI-induced enterocolitis is very different to ulcerative colitis (UC), and that unlike UC, it is reversible with limited treatment options. Therefore, they would expect that the likely expected gain in benefits would be higher for patients with ICI-induced enterocolitis. <p>The group also identified there was insufficient evidence presented to compare the value of vedolizumab with infliximab for the treatment of grade 2 enterocolitis, and to be confident that the anticipated additional benefits justified the additional anticipated extra costs.</p> <p>OWMAG were unable to reach a decision on cost-effectiveness.</p>
Budget impact	<p>OWMAG consider the clinical estimate of patient numbers reported to be reasonable.</p> <p>Clinicians in Wales estimate that 2 extra patients with grade 2 enterocolitis would be eligible for treatment with vedolizumab per year in addition to the 10 patients with grade 3–4 enterocolitis estimated in the original assessment, thereby giving 12 patients in total. This compares to the 5 patients treated with vedolizumab for grades 2-4 enterocolitis in Wales in 2023.</p> <p>The group note that mortality rates and additional screening and monitoring for bacterial, viral and fungal infections and adverse event costs have not been included in the budget impact.</p> <p>OWMAG acknowledge that a proportion of patients with grade 2 ICI-induced enterocolitis in Wales are already receiving vedolizumab through local agreement routes. Also, as ICI usage grows, it is acknowledged that patient</p>

	<p>numbers are anticipated to increase over the coming years, resulting in additional budgetary impact in Wales. This will be monitored as part of the review process.</p> <p>OWMAG consider that the base case provided in the report is a reasonable estimate of the associated cost to NHS Wales.</p>
Other factors	<p>OWMAG acknowledges that although grade 2 colitis is milder than grade 3, it can still significantly impact patients' quality of life. This may include malnutrition, poor sleep, inability to work, lethargy and chronic dehydration. In addition, OWMAG also acknowledge that long term and/or high dose steroid exposure is associated with increased risk of a wide range of adverse effects including infections, fractures, high blood sugar, cardiovascular and cerebrovascular events and that there are clinical, cost and quality of life benefits in reducing steroid burden and repeated exposure to corticosteroids. It was noted that many patients are elderly and these effects may be more severe. The use of vedolizumab may help a rapid wean from steroids.</p> <p>OWMAG also considers that earlier intervention and resolution of enterocolitis enables resumption of cancer treatment with ICIs for the majority of patients which offers an increased possibility of durable outcomes.</p> <p>As vedolizumab targets the gut and has no identified systemic immunosuppressive activity, clinicians suggest this may offer potential benefits over infliximab, especially for patients with high disease burden and fewer cancer treatment options.</p> <p>There are no licensed alternative treatment options routinely available.</p>
Final recommendation	<p>OWMAG recommends that the existing recommendation for the use of off-label vedolizumab (Entyvio®) for the treatment of ICI-induced grade 3-4 enterocolitis where symptoms have not responded to first line immunosuppression with corticosteroids and infliximab, or when infliximab is unsuitable and as outlined in OW22 be updated to include the expanded indication considered in this reassessment. Therefore, the updated recommendation is as follows:</p> <p>Vedolizumab can be made available within NHS Wales:</p> <ul style="list-style-type: none"> • for the treatment of ICI-induced grade 3-4 enterocolitis, where symptoms have not responded to first line immunosuppression with corticosteroids and infliximab or when infliximab is unsuitable

	<ul style="list-style-type: none"> • for the treatment of ICI-induced grade 3–4 enterocolitis in patients who are corticosteroid-dependent requiring multiple challenges with corticosteroids when symptoms have not responded to infliximab or when infliximab is unsuitable • as an option for the treatment of ICI-induced grade 2 enterocolitis, where symptoms have not responded to first line immunosuppression with corticosteroids or for patients who are corticosteroid-dependent requiring multiple challenges with corticosteroids <p>This recommendation is subject to the development of appropriate start/stop criteria.</p>
Summary of rationale	<p>There is some limited evidence to support the use of vedolizumab as an clinically effective option for the treatment of ICI-induced grade 2 enterocolitis, where symptoms have not responded to first line immunosuppression or who are steroid-dependent and require multiple treatment courses with steroids for relapses and for the treatment of ICI-induced grade 3–4 enterocolitis in patients who are corticosteroid-dependent requiring multiple challenges with corticosteroids when symptoms have not responded to infliximab or when infliximab is unsuitable.</p> <p>There are no licensed alternative treatment options and recent updates to international guidelines recommend the use of vedolizumab for the treatment of grade 2 enterocolitis unresponsive to corticosteroids. Allowing the use of vedolizumab earlier in the pathway may prevent the worsening of symptoms, lessen steroid burden by allowing rapid steroid weaning, allow resumption of ICIs to treat the patient’s cancer and maintain or improve the quality of life. There was insufficient evidence to recommend using vedolizumab, which has a higher acquisition cost, before infliximab for patients with grade 2 disease. Therefore, vedolizumab is recommended as an option and clinicians should be mindful of both the associated costs and benefits of both treatments before agreeing which treatment to use.</p> <p>A proportion of the extended patient population in Wales is already receiving this treatment via local agreement routes, supporting the extension on an All Wales basis would ensure equity of access. The review after 12 months will provide more clarity around patient numbers and the number of doses of vedolizumab administered.</p>